REMARKS

Claims 1, 4, 7, and 18-26 are pending in the application. No amendments have been made by the present response.

35 U.S.C. § 112, Second Paragraph (Indefiniteness)

At pages 2-3 of the Office Action, claims 4, 19, 22, and 25 were rejected as allegedly indefinite. With respect to independent claim 4, the Examiner stated that "[i]t is unclear from the current phrasing of the claim how the increase in glucose uptake in a mammalian cell is linked with contacting a candidate agent with a SMCE-regulating factor." In addition, the Examiner stated that "it is unclear what Applicant intends to encompass by 'SMCE-regulating factor' in claim 4." Claims 19, 22, and 25 were rejected under this heading because they depend directly or indirectly from claim 4.

Applicants respectfully traverse the rejection in view of the following remarks.

Claim 4 contains two "determining" steps: (i) determining whether a candidate agent stimulates a function of a SMCE-regulating factor; and (ii) determining whether the candidate agent increases glucose uptake in a mammalian cell. In the first "determining" step, a determination is made of whether the candidate agent stimulates a function of the SMCE-regulating factor. This step can be performed using any system (e.g., cell-based or cell-free) that permits an evaluation of a function of a SMCE-regulating factor. In the second "determining" step, a determination is made of whether the candidate agent increases glucose uptake in a mammalian cell. Because of the "in a mammalian cell" limitation, this step must be performed in a cell-based system that assesses the effect of the candidate agent on the mammalian cell. These two steps are directly related to the inventors' discovery indicating that an increase in SMCE results in increased insulin-mediated glucose uptake. The person of ordinary skill in the art would understand the connection between the two steps and would therefore have no difficulty ascertaining the metes and bounds of claim 4.

An SMCE-regulating factor is any factor that regulates store-mediated Ca^{2+} entry in a cell. An SMCE-regulating factor can be a polypeptide, examples of which are described in the

specification at page 5, lines 16-20. Claim 4 requires "determining whether the candidate agent stimulates a function of the SMCE-regulating factor." As noted in the specification, functions of an SMCE-regulating factor include altering Ca^{2+} entry and glucose uptake in a cell.

In view of the foregoing remarks, applicants request that the Examiner withdraw the indefiniteness rejection of claims 4, 19, 22, and 25.

35 U.S.C. § 102(b) (Anticipation)

At pages 3-4 of the Office Action, claims 1, 4, 7, and 18-26 were rejected as allegedly anticipated by Westfall et al. (1990) Am. J. Physiol. 258:R462-68 ("Westfall").

Applicants respectfully traverse the rejection in view of the following remarks.

The claimed invention is based, at least in part, upon the inventors' surprising discovery that inhibition of "store-mediated" Ca^{2+} entry (SMCE) results in a decrease in insulin-stimulated glucose uptake in skeletal muscle. This finding supports a physiological role of SMCE in insulin action in skeletal muscle, where an increase in SMCE results in an increased insulin-mediated glucose uptake. Consistent with the inventors' discovery, the claims are directed to methods for identifying compounds that increase SMCE as agents that increase cellular glucose uptake. Each of independent claims 1, 4, and 7 contains a step of determining whether an agent that increases SMCE (or stimulates a function of a SMCE regulating factor) increases glucose uptake in a cell.

Westfall describes the ability of agonists and antagonists of L-type calcium channels to modulate basal and insulin-mediated skeletal muscle sugar transport. Westfall states that a low concentration of the compound BAY K 8644 (an agonist of L-type calcium channels) enhanced insulin-stimulated skeletal muscle sugar transport, whereas a high concentration of the compound led to a diminished ability of insulin to stimulate sugar transport. Westfall nowhere describes compounds that increase SMCE or the use of SMCE-stimulating compounds to increase cellular glucose uptake. Because each of the independent claims contains a step of determining whether an agent that increases SMCE (or stimulates a function of a SMCE regulating factor) increases glucose uptake in a cell, Westfall does not anticipate any of the claimed methods.

In view of the foregoing remarks, applicants respectfully request that the Examiner withdraw the anticipation rejection of claims 1, 4, 7, and 18-26.

35 U.S.C. § 103(a) (Obviousness)

At pages 4-5 of the Office Action, claims 1, 4, 7, and 18-26 were rejected as allegedly unpatentable over Westfall.

Applicants respectfully traverse the rejection in view of the following remarks.

As detailed above, Westfall describes the ability of agonists and antagonists of L-type calcium channels to modulate basal and insulin-mediated skeletal muscle sugar transport. However, nothing in Westfall suggests that SMCE is involved in insulin-stimulated glucose uptake in skeletal muscle. The claimed invention relates to SMCE as a stimulator of glucose uptake and is supported in part by the inventors' discovery that application of SMCE inhibitors to skeletal muscle caused a dose-dependent decrease insulin-stimulated glucose uptake. Westfall does not report any experimental findings describing an effect of SMCE stimulators or inhibitors on glucose uptake. Furthermore, Westfall's findings with L-type calcium channel agonists and antagonists provide no suggestion that SMCE inhibitors would cause a decrease in insulin-stimulated glucose uptake (or that compounds that increase SMCE will increase cellular glucose uptake). As noted above, all of the pending claims contain a step of determining whether an agent that increases SMCE (or stimulates a function of a SMCE regulating factor) increases glucose uptake in a cell. The effect of SMCE inhibitors on glucose uptake was discovered by the inventors and was not described or suggested by Westfall. Because Westfall does not suggest that increasing SMCE in a cell will result in an increase in glucose uptake in the cell, the reference does not render obvious any of the claimed methods.

In view of the foregoing remarks, applicants respectfully request that the Examiner withdraw the obviousness rejection of claims 1, 4, 7, and 18-26.

CONCLUSIONS

Applicants submit that all grounds for rejection have been overcome, and that all claims are now in condition for allowance, which action is requested.

Please apply any charges or credits to deposit account 06-1050, referencing Attorney Docket No. 13425-115001.

Respectfully submitted,

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Jack Brennan
Reg. No. 47,443

Fish & Richardson P.C.
Citigroup Center
52nd Floor
153 East 53rd Street
New York, New York 10022-4611
Telephone: (212) 765-5070
Facsimile: (212) 258-2291

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